

Research Review: A systematic review and meta-analysis of sex/gender differences in social interaction and communication in autistic and nonautistic children and adolescents

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Background: Evidence increasingly suggests that ASD manifests differently in females than males. Previous reviews investigating sex/gender differences in social interaction and social communication have focused at the level of broad constructs (e.g. comparing algorithm scores from pre-existing diagnostic instruments) and have typically reported no significant differences between males and females. However, a number of individual studies have found sex/gender differences in narrow construct domains. **Methods:** We conducted a systematic review and random effects model meta-analyses (in January 2019 and updated January 2020) that investigated sex/gender differences in narrow construct measures of social communication and interaction in autistic and nonautistic children and adolescents, and adults. Study quality was appraised using the Appraisal Tool for Cross-Sectional Studies (AXIS, *BMJ Open*, 6, 2016, 1). **Results:** Across 16 studies (including 2,730 participants), the analysis found that female (vs. male) individuals with ASD had significantly better social interaction and social communication skills (SMD = 0.39, $p < .001$), which was reflective of a similar sex/gender profile in nonautistic individuals (SMD = 0.35, $p < .001$). Nonautistic males had significantly better social interaction and communication than males with ASD (SMD = 0.77, $p < .001$). Nonautistic females also had significantly better social interaction and communication than females with ASD (SMD = 0.72, $p < .001$). Nonautistic males had better social interaction and communication than females with ASD, though this difference was not significant (SMD = 0.30, $p = .07$). **Conclusions:** This systematic review and meta-analysis highlighted important sex/gender differences in social interaction and communication for individuals with ASD, likely not captured by pre-existing diagnostic instruments, which potentially contribute to the under recognition of autism in females, and may need to be reflected in the diagnostic process. **Keywords:** Autism spectrum disorders; sex differences; gender difference; DSM; meta-analysis.

Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disability characterized by ‘persistent impairment in reciprocal social communication and social interaction, and restricted, repetitive patterns of behaviour, interests or activities’ (American Psychiatric Association, 2013, p. 53). As researchers have not yet been able to separate the effects of sex and gender on ASD presentation, the term ‘sex/gender’ is used throughout this paper to acknowledge the overlap between the two (Lai, Lombardo, Auyeung, Chakrabarti, & Baron-Cohen, 2015; Springer, Stellan, & Jordan-Young, 2012). In accordance with research suggesting there is no one preferred way of describing ASD within the broader ASD community, both person-first and identity-first language will be used (Kenny et al., 2016). Approximately 2% of the childhood population has a diagnosis of ASD (Maenner et al., 2020). The reported sex/gender ratio in ASD varies depending on the specific demographics – such as IQ – of the participants included in the study

(Maenner et al., 2020). On average, an approximate ratio of four males to every female child and adolescents are given an ASD diagnosis (Fombonne, 2009; Maenner et al., 2020).

Loomes, Hull, and Mandy (2017) conducted a meta-analysis and compared active case-finding methods (i.e. studies which first screen a population in order to identify at-risk children, who then undergo professional diagnostic assessment) with passive case-finding methods (i.e. studies that review existing databases or contact parents to identify whether children have received a diagnosis of ASD). They found that the male-to-female ratio was significantly smaller in active case-finding studies than passive case-finding studies (3.25 vs. 4.56). This difference suggests there is a diagnostic gender bias, such that there are females not known to clinical services but who, if assessed, would potentially meet diagnostic criteria for ASD (Loomes et al., 2017). This diagnostic gender bias has a number of potential sources, including the proposition of a distinct autistic female phenotype (Hull, Petrides, & Mandy, 2020 for a review). It is argued, for example, that higher levels of camouflaging behaviours (i.e.

Conflict of interest statement: No conflicts declared.

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strategies to appear less autistic in social interactions) contribute to an under recognition of autism in females (e.g. Hull, Mandy, & Petrides, 2017; Hull et al., 2019; Wood-Downie et al., 2020). With respect to diagnostic bias, it is suggested that professionals may hold gender-based stereotypes (e.g. that autism is a male-condition) or differentially interpret behaviour (e.g. social withdrawal perceived as shyness in females, but an indicator of autism in males), meaning autism may be under-recognized in females, which has recently gained some empirical support (Whitlock, Fulton, Lai, Pellicano, & Mandy, 2020).

Sex/gender bias in ASD diagnostic criteria and instruments

Reliable physiological and/or genetic biomarkers are yet to be identified for ASD (Goldani, Downs, Widjaja, Lawton, & Hendren, 2014). Consequently, diagnostic criteria are based predominantly on behavioural descriptors, such as difficulties with social-emotional reciprocity (APA, 2013). Current 'gold-standard' diagnostic instruments, such as the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2, Lord et al., 2012) and Autism Diagnostic Interview-Revised (ADI-R, 2003; Rutter, Le Couteur, & Lord, 2003), have been developed and validated predominantly using samples of male individuals, raising the possibility that the formation of items underpinning diagnosis may be biased towards a male manifestation of the condition (Kirkovski, Enticott, & Fitzgerald, 2013; Kreiser & White, 2014; Lai et al., 2015). For example, the validation sample for the original ADOS consisted of 170 males and only 36 females with ASD (Lord et al., 2000). In addition, McCrimmon and Rostad (2013) noted that the standardization sample for the ADOS-2 was predominately male and was mainly recruited through clinics, meaning that an ascertainment bias may be present via the exclusion of females who have not yet come to clinical attention.

More importantly, when used diagnostically, these instruments have been found to miss a disproportionate number of female (vs. male) individuals with ASD. Lai et al., (2011) found that only 21% of adult females diagnosed with ASD in childhood met ADOS cut-off scores, compared with 58% of males, despite similarly low social-cognitive ability between genders. Consistently, Russell, Steer, and Golding (2011) analysed a longitudinal UK cohort study and found that girls with similar levels of autistic traits to boys, were significantly less likely to receive an ASD diagnosis. Further evidence has found that females with higher IQ were significantly less likely than males to meet diagnostic criteria on the ADI-R (Ratto et al., 2018). In addition, girls (but not boys) who met

diagnostic criteria showed higher levels of behavioural and/or cognitive difficulties than nonautistic peers with similarly high levels of autistic traits (Dworzynski, Ronald, Bolton, & Happé, 2012).

Overall, these findings indicate that the diagnostic criteria are biased towards a male-specific manifestation of ASD and suggest that female children and adolescents may be missed in the diagnostic process, and particularly if they do not present with comorbid behavioural or cognitive difficulties. This research may also partly account for why girls/young women are often referred and given a diagnosis of ASD on average later than boys/young men (e.g. Rutherford et al., 2016).

Broad and narrow constructs in ASD

Deficits with social communication and interaction are one of the two core areas of difficulty from the DSM-5 ASD diagnostic criteria (APA, 2013). These areas are broken down into three subdomains: (a) deficits in social-emotional reciprocity, (b) deficits in nonverbal communicative behaviour used for social interaction and (c) deficits in developing, maintaining and understanding relationships. Social interaction and communication difficulties can be measured at either the level of 'broad' or 'narrow' construct (Lai et al., 2015). Broad constructs, including the DSM-5 criteria of deficits in social interaction and communication, define ASD abstractly. In contrast, narrow constructs are fine-grained subdomains of broad constructs that include the subdomains outlined above (e.g. deficits in social-emotional reciprocity), as well as associated psychological constructs (e.g. social attention), and co-occurring issues (e.g. social anxiety). Each narrow construct has a range of associated behavioural exemplars, such as difficulties engaging in back-and-forth conversations, atypical eye gaze patterns and specific types of anxiety symptoms.

Reviews investigating sex/gender differences in social interaction and communication at the level of broad construct often find no sex/gender differences (Lai & Szatmari, 2020). For example, a meta-analysis by van Wijngaarden-Cremers et al. (2014) found no significant differences between autistic male and female individuals in the core domains of social interaction and communication, both across the sample as a whole, and when split into five different age categories (toddlers, preschoolers, children, adolescents and adults). Two further meta-analyses similarly reported no significant differences between autistic male and female children and adolescents in terms of social interaction and communication difficulties (Mahendiran et al., 2019) or children, adolescents and adults (Hull et al., 2017). Two recent and relatively large-scale studies ($N = 967$) also found autistic males and female individuals (ages

ranged from 1 to 56 years) had similar overall social communication and interaction difficulties (Mussey, Ginn, & Klinger, 2017; Ratto et al., 2018).

Existing studies have typically employed pre-existing diagnostic instruments – predominantly the ADOS-2 and ADI-R – and often report overall social interaction and communication scores (i.e. at the broad construct level). Because these instruments have been developed largely from samples of autistic males, they may not be sensitive to the way in which ASD manifests in female individuals (Hull & Mandy, 2017; Lai & Szatmari, 2020). To overcome these limitations, Lai et al. (2015) and Lai and Szatmari (2020) recommended that sex/gender differences in ASD should be investigated by focusing on narrow constructs and behavioural exemplars of social communication and interaction, rather than by comparing algorithm scores from pre-existing diagnostic instruments.

In support of this focus, research using narrow social and communication constructs has demonstrated sex/gender differences. For example, girls with ASD were found to have higher levels of peer engagement on the playground (Dean, Harwood, & Kasari, 2016), increased social motivation (Head, McGillivray, & Stokes, 2014) and social reciprocity (van Ommeren, Koot, Scheeren, & Begeer, 2017), and showed a greater use of pragmatic language markers (Parish-Morris et al., 2017). Friendships may also be experienced differently, with autistic girls more likely to be overlooked by peers than autistic males, who are more likely to be rejected (Dean et al., 2014).

Current study

The current systematic review and meta-analysis investigated sex/gender differences in narrow constructs and associated behavioural exemplars of social interaction and communication, based on DSM-5 symptom subdomains not measured using diagnostic/screening instruments. This analysis builds on existing research to address issues with diagnostic bias, as well as our understanding of the contradictory findings associated with reviews based upon broad constructs (that typically find minimal sex/gender differences), and individual studies based on narrow constructs which have found sex/gender differences. If the diagnostic profile of autistic male and female individuals differs in terms of social interaction and communication at the narrow construct/behavioural exemplar level, then diagnostic criteria should reflect these differences. Finally, based on previous theory and evidence which suggests developmental differences may moderate the effects of sex/gender differences, we also aimed to investigate whether sex/gender differences are influenced by age, (e.g. Hull et al., 2017; Lai et al., 2015; Van Wijngaarden-Cremers et al., 2014).

The systematic review/meta-analysis addressed the following three questions:

1. Are there any sex/gender differences in narrow construct subdomains of the DSM-5 ASD diagnostic criteria of social interaction and communication?
2. If found, do autistic sex/gender differences mirror those found in nonautistic individuals?
3. Does age moderate the effects of any potential sex/gender differences?

Given the exploratory nature of the meta-analysis, no *a priori* hypotheses were formulated.

Method

This review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA, Moher, Liberati, Tetzlaff, & Altman, 2009) and was preregistered on Prospero (registration number: CRD42019120804).

Search

A search of the databases PsychINFO, Medline, Psych Articles, CINAHL (Plus with Full Text) and PubMed databases was conducted on 23 January 2019 and updated on 24 January 2020, based upon the DSM-5 ASD symptom subdomains of social interaction and communication, including the population terms 'autis*' and 'ASD'; comparator terms 'sex difference*' and 'sex/gender difference*'; and outcome terms 'social reciprocity', 'conversation', 'turn-taking', 'eye contact', 'friend*' and 'nonverbal communication' (see Table S1 for full search terms). No language restrictions were applied. In addition, reference lists of included studies were hand-searched to detect any pertinent study possibly missed with the electronic search. This process was first conducted by the first author. To minimize bias, the second author independently completed title and abstract screening for 187 randomly selected studies and 23 randomly selected studies for full-text screening. Interobserver agreement was 97% for title and abstract screening and 96% for full-text screening. Discrepancies were discussed until a consensus was reached.

Eligibility criteria

Table 1 provides the rationale for each inclusion and exclusion criterion and further details (i.e. specific examples of the types of outcome measures and instruments that were excluded) can also be found in Appendix S1.

Data extraction

We extracted data on sample characteristics (e.g. gender, age of participants; diagnostic criteria used) and outcomes related to social interaction and/or communication narrow constructs. We did not have an *a priori* search list of measures. Instead, we used a data-driven approach and the measures were identified through the search process, based on our *a priori* inclusion and exclusion criteria. We contacted corresponding authors if social interaction and/or communication means and standard deviations were not available in the reported data. The first and second author extracted data (number of participants, age of participants, means and standard deviations of outcome measures) and independently entered items. Interobserver agreement ranged from 92% to 98%, and discrepancies were discussed until a consensus was reached.

Table 1 Rationale for inclusion and exclusion criteria

	Rationale
Inclusion criteria	
Quantitative cross-sectional studies	The review considered whether there were quantifiable differences between male and female individuals with and without ASD
Peer reviewed studies	Publication bias was assessed using funnel plots
Studies with both autistic and nonautistic males and females	To understand the implications of the results for diagnostic criteria, it was important to determine whether sex/gender differences in autistic individuals were also found in nonautistic individuals
Studies that included a subdomain (narrow construct) of the APA (2013) ASD diagnostic criteria of social interaction and communication	Previous sex/gender difference reviews and meta-analyses (e.g. Hull et al., 2017) have predominantly been based on broad construct measures of social interaction and communication. However, there is a growing body of research investigating sex/gender differences in narrow construct domains. To date, there has been no attempt to systematically review studies that have only incorporated narrow construct measures of social interaction and communication
Exclusion criteria	
Studies with ≤ 7 autistic females or males	A sufficient number of participants in each group was needed to allow for statistical comparisons
Studies with outcomes based on diagnostic/screening instruments	Current diagnostic/screening instruments may not be sensitive to the ASD female phenotype and therefore may not capture sex/gender differences. For example, the formation of items within these instruments may have been biased by the small amount of females (relative to males) included within their development and validation

Study quality appraisal

The focus of the review was cross-sectional studies; therefore, the quality of included studies was appraised using the Appraisal Tool for Cross-Sectional Studies (AXIS, Downes, Brennan, Williams, & Dean, 2016). Due to the lack of an appraisal tool for cross-sectional studies, the AXIS was developed through an international Delphi panel of 18 medical and veterinary experts; following three rounds of the Delphi process, there was consensus (81%) that all components were appropriate for nonexperts. The AXIS tool consists of 20 questions, which require an answer of 'yes', 'no' or 'do not know'; score range = 0–20, with higher scores reflecting higher quality studies. Questions relate to the rationale for the study (were the aims/objectives of the study clear?), methods (e.g. was the sample size justified?), results (e.g. were the basic data adequately described?), discussion (e.g. were the limitations of the study discussed) and other aspects of studies (e.g. were there any funding sources or conflicts of interest that may affect the authors' interpretation of the results?). The first and second authors independently rated all studies and agreement was 96%.

Data analysis

Random effects model meta-analyses were performed using Review Manager 5.3 (The Cochrane Collaboration, 2014) for narrow construct measures of social interaction and communication. Standardized mean differences (SMD) were calculated for the following comparisons: (a) autistic males and females, (b) nonautistic males and females, (c) autistic and nonautistic males, (d) autistic and nonautistic females and (e) autistic females and nonautistic males. Where multiple measures were used in one study, pooled means and standard deviations were used when the measures reflected one individual construct (e.g. different scales from the same questionnaire or observational measure). Alternatively, the measures most similar to other studies were included (Table 2). Where heterogeneity tests were significant, a subgroup analysis was conducted to test for differences between studies that included only infants and/or children (<12 years), children and/or adolescent (12–19 years), and adult participants (>19 years).

Results

Search results

Search results are presented in Figure 1, and further information (e.g. how many separate hits were produced in our original and updated search) can be found in Appendix S2. References and reasons for full-text article exclusion can be found in Table S2.

Characteristics of included studies

The characteristics of included studies in the quantitative review are presented in Table 2. Peer relationships was the most frequent outcome measure ($n = 6$). Other studies measured play behaviours ($n = 2$), social attention ($n = 3$) and social reciprocity ($n = 1$). The majority of studies included children and/or adolescents ($n = 8$) or infants and/or children ($n = 5$). Diagnoses were confirmed in the majority ($n = 13$) of studies, usually via clinical assessment and/or ADOS assessment ($N = 11$). $N = 9$ studies used questionnaire data (Baron-Cohen & Wheelwright,

Table 2 Characteristics of included studies

Authors (date)	Study characteristics							Autistic		Nonautistic			
	Narrow construct/behavioural exemplar assessed	Measure used for Meta-Analysis (age classification for moderator analysis)	Diagnoses at the time of study	Total FQ score (adult)	AS/HFA (proportions not reported)	How diagnosis confirmed	Males (n)	Females (n)	Mean age (years)	Males (n)	Females (n)	Mean age (years)	AXISScore
Baron-Cohen and 40	Wheelwright (2003)	Peer relationships	Total FQ score (adult)	AS/HFA (proportions not reported)	DSM-IV criteria for ASD/AS	Not reported	17	34.4	51	17	34.4	27	49
Chawarska et al. (2016)	Social attention	Mean proportion of time spent looking at faces averaged from 6, 9, and 12 months (infants/children)	Siblings of children with ASD (100%)	N/A	ADOS	71	30	0.75	32	29	0.75	13	13
Cheng et al. (2017)	Interpersonal motor synchrony	Mean PTSR (adult)	N/A	N/A	AQ	19	19	29.1	28	17	32	12	12
Dean et al. (2014)	Peer relationships	Mean of social preferences, acceptance, and connections of FS (infants/children)	ASD (100%)	Not reported	Clinician assessment and ADOS	25	25	7.5	25	25	7.8	14	14
Dean et al. (2016)	Peer engagement behaviours	Mean of Games, Joint engage, and Solitary scores of POPE (infants/children)	ASD (100%)	Not reported	ADOS-2	24	24	7.7	24	24	7.9	14	14
Harrop et al. (2017)	Play behaviours	Highest level of play reached (infants/children)	ASD (100%)	Not reported	ADI-R/ADOS	14	14	3.8	14	12	2	15	15
Harrop et al. (2018)	Social attention	Average preference to face, with and without CI object (infants/children)	ASD (100%)	Not reported	SCQ and mixture of clinician assessment, ADOS, ADI-R and CARS	23	22	9.0	16	16	7.8	14	14
Head et al. (2014)	Peer relationships	Average FQ scores, based on child/adolescent report (children/adolescents)	ASD (not including LFA or PDD-NOS; 100%)	Not reported	Not reported	25	25	13.7	26	25	12	13	13

(continued)

Table 2 (continued)

Authors (date)	Narrow construct/ behavioural exemplar assessed	Study characteristics					Autistic		Nonautistic			
		Measure used for Meta-Analysis (age classification for moderator analysis)	Diagnoses at the time of study	Diagnostic criteria used	How diagnosis confirmed	Males (n)	Females (n)	Mean age (years)	Males (n)	Females (n)	Mean age (years)	AXISScore
Horiuchi et al. (2014)	Peer difficulties	Total peer problems score of SDQ (children/ adolescents)	ASD (100%)	DSM-IV-TR criteria for ASD	Clinician assessment	129	44	7.9	129	44	7.9	13
Knickmeyer et al. (2007)	Play behaviours	Average of all play scores (children/ adolescents)	Of those available (91% of total sample): AS (32%), ASD (58%), HFA (3%), PDD-NOS (3%), Atypical ASD (2%)	ICD-10 or DSM-IV	Not reported	46	20	10.2	31	24	5.1	14
O'Connor et al. (2019)	Social attention	Looking behaviour (children/ adolescents)	Not reported	DSM-IV-TR criteria	Clinician assessment and ADI-R	72	16	12.4	60	85	12.5	13
Parish-Morris et al. (2017)	Social pragmatic hesitation markers	UM ratio (children/ adolescents)	ASD (100%)	DSM-IV-TR criteria for ASD	Clinician assessment, ADOS and ADI-R	49	16	10.0	8	9	11.3	13
Sedgewick et al. (2016)	Peer relationships	Average FQS scores (children/ adolescents)	ASD (83%); AS (17%)	DSM-IV-TR or ICD-10 criteria for ASD/AS	Clinician assessment and Statement of Special Educational Needs indicating ASD	10	13	13.9	10	13	13.8	13
Sedgewick et al. (2018)	Peer relationships	Average FQS scores (children/ adolescents)	ASD (100%)	DSM-IV-TR or DSM-5 or ICD-10 criteria for ASD/AS/ ASD	Clinician assessment, ADOS-2 and SRS	26	27	14.4	23	26	14.4	13
Sedgewick et al. (2019)	Peer relationships	Total FQ scores (adult)	Not reported	Not reported	Self-report	72	317	35.6	54	327	32.4	14
van Ommeren et al. (2017)	Social reciprocity	Total IDT scores (children/ adolescents)	AD (22%), AS (8%), PDD-NOS (56%), MCDD (1.4%)	DSM-IV-TR criteria for ASD	Clinician assessment and SRS	114	32	13.8	55	24	11.4	13

Appendix S3 for table note.

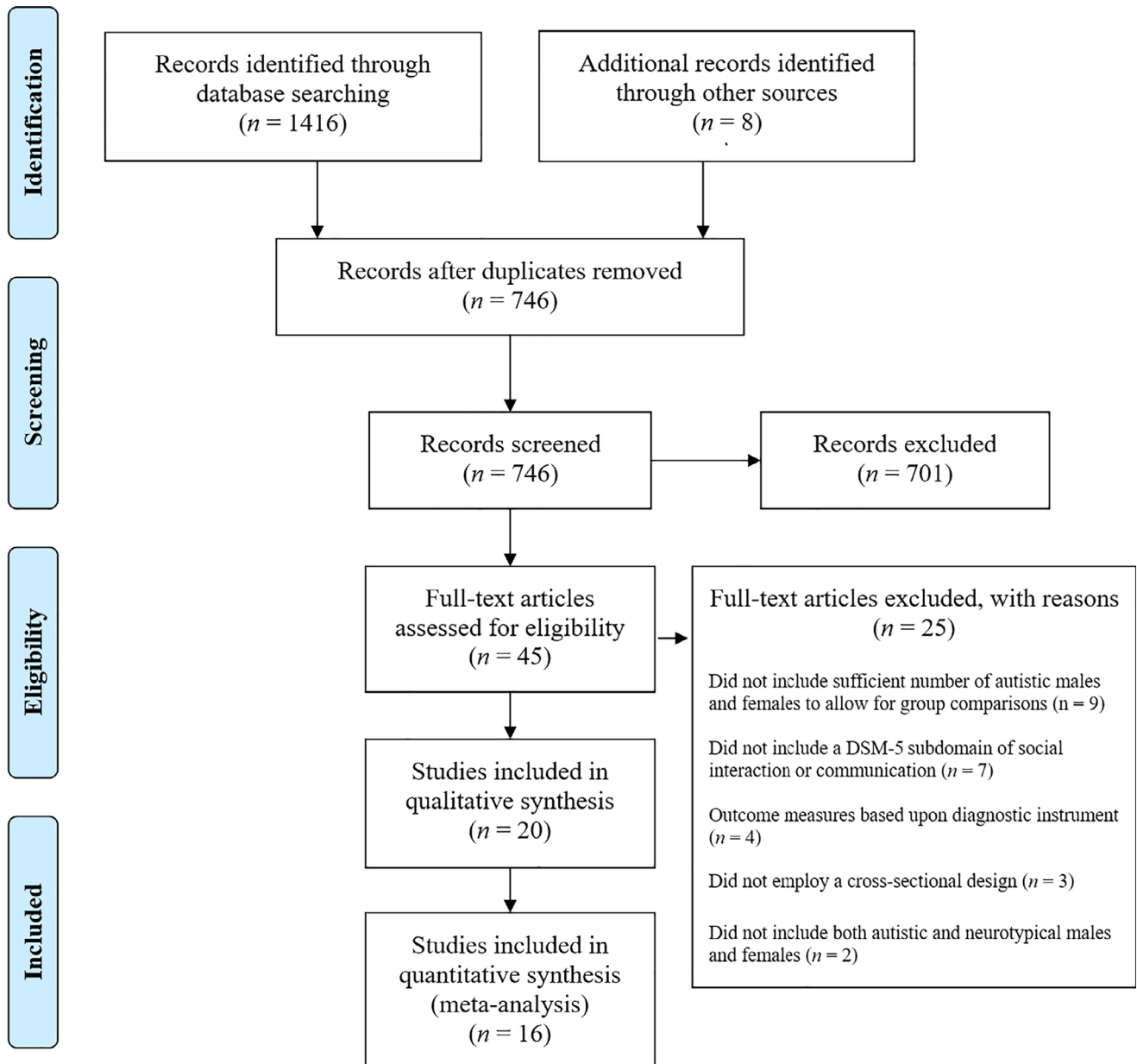


Figure 1 PRISMA flow diagram of study identification and selection

2003; Dean et al., 2014; Harrop, Green, & Hudry, 2017; Head et al., 2014; Horiuchi et al., 2014; Knickmeyer, Wheelwright, & Baron-Cohen, 2007; Sedgewick, Hill, & Pellicano, 2018; Sedgewick, Hill, Yates, Pickering, & Pellicano, 2016; Sedgewick, Leppanen, & Tchanturia, 2019). Further studies used a range of different behavioural measures/tasks, including use of eye-tracking to measure social attention (Chawarska, Macari, Powell, Dinicola, & Shic, 2016; Harrop et al., 2018) and a novel drawing task to measure social reciprocity (van Ommeren et al., 2017).

Measurements across 10 studies corresponded to the DSM-5 subdomain of developing, maintaining and understanding relationships (Baron-Cohen & Wheelwright, 2003; Dean et al., 2014, 2016; Harrop et al., 2017; Head et al., 2014; Horiuchi et al., 2014; Knickmeyer et al., 2007; Sedgewick et al., 2016, 2018, 2019),

four to nonverbal communicative behaviour (Chawarska et al., 2016; Harrop et al., 2018; O'Connor, Stockmann, & Rieffe, 2019; Parish-Morris et al., 2017) and two to social-emotional reciprocity (Cheng, Kato, & Tseng, 2017; van Ommeren et al., 2017).

Study quality

Table 2 shows that the scores for studies in the current review ranged from 12 to 15 out of 20. Further details of study quality can be found in Appendix S4.

Publication bias

Egger's test was significant ($p = .02$) for the comparison between autistic males and females, suggesting

publication bias was present, though appeared only marginally asymmetrical when visually inspecting the funnel plot (Figure S1). It was not possible to calculate Egger's test for the other four comparisons because there were fewer than ten studies in the subgroups. Three of the remaining plots (autistic and nonautistic males; autistic and nonautistic females; autistic females and nonautistic males) showed marginal signs of asymmetry (Figures S2, S3 and S5). The studies that were missing for the comparisons between autistic and nonautistic males and autistic and nonautistic females were in line with the main findings (i.e. higher scores in nonautistic males and females relative to autistic males and females), suggesting that the overall pattern of results would be the same if they were included. The final plot (nonautistic male and females) shows that most studies clustered around the overall SMD, suggesting publication bias was not evident (Figure S4).

Comparison of autistic males and females

Figure 2 shows significantly better social communication and interaction skills in autistic females (compared with autistic males) (SMD = 0.39, 95% Confidence Interval (CI) = (0.26, 0.53), $p < .001$). Heterogeneity tests were nonsignificant, $\chi^2(15) = 17.33$, $p = .30$, indicating that across studies the pattern of results was similar.

Comparison between nonautistic males and females

Figure 3 shows that nonautistic females had significantly better social communication and interaction than nonautistic males (SMD = 0.35, 95% CI = (0.17, 0.54), $p < .001$), though heterogeneity tests were significant ($\chi^2(15) = 29.87$, $p = .01$). The moderating effect of age was significant ($\chi^2(2) = 9.92$, $p = .007$): females had better social communication and interaction skills than males for all three age groups, and the SMD between females and males increased with age (SMD infants/children < SMD children/adolescents < SMD adults). Heterogeneity tests were nonsignificant for the three subgroups, suggesting that developmental differences explained heterogeneity when all studies were included.

Comparison between autistic and nonautistic males

Figure 4 indicates that nonautistic males had significantly better social interaction and communication than autistic males (SMD = 0.77, 95% CI (0.47, 1.06), $p < .001$), though heterogeneity tests were significant ($\chi^2(15) = 86.70$, $p < .001$). The moderating effect of age was nonsignificant ($\chi^2(2) = 3.95$, $p = .14$), with nonautistic males having better social communication and interaction skills than autistic males for all three age groups to a similar degree (i.e., the SMD was similar for the three age groups).

Comparison between autistic and nonautistic females

Figure 5 shows that nonautistic females had significantly better social interaction and communication than autistic females (SMD = 0.72, 95% CI (0.32, 1.12), $p < .001$), though heterogeneity tests were significant ($\chi^2(15) = 139.07$, $p < .001$). The moderating effect of age was significant ($\chi^2(2) = 15.11$, $p < .001$): Nonautistic females had better social communication and interaction skills than autistic females for all three age groups and the SMD between them increased with age (SMD infants/children < SMD children/adolescents < SMD adults). Heterogeneity tests, however, remained significant for infants/children and children/adolescents, suggesting other moderators may also be affecting the differences between studies.

Comparison between autistic females and nonautistic males

Figure 6 shows that nonautistic males had better social interaction and communication than autistic females, but this difference was not significant (SMD = 0.30, 95% CI (-0.03, 0.63), $p = .07$); however, heterogeneity tests were significant ($\chi^2(15) = 88.55$, $p < .001$). The moderating effect of age was nonsignificant ($\chi^2(2) = 0.82$, $p = .66$), with nonautistic males having nonsignificantly better social communication and interaction skills than autistic females for all three age groups to a similar degree (i.e., the SMD was similar for the three age groups).

Discussion

This systematic review and meta-analysis investigated sex/gender differences in social interaction and communication in autistic and nonautistic individuals across 16 studies. It also considered whether potential differences in autistic individuals were similar to those evident in nonautistic individuals, and if age moderated any difference. To overcome potential sex/gender diagnostic bias, we focused exclusively on narrow construct domains of social interaction and communication, rather than broad construct measures typically reflected in 'gold-standard' instruments. The review showed that there were a broad range of different outcome measures employed across studies (e.g. social attention; peer relationships; play behaviours). Most studies ($n = 9$) used questionnaires to measure social interaction and communication skills, with the remainder of studies using eye-tracking, observational measures or behavioural tasks. The meta-analysis indicated that autistic females demonstrated significantly better social interaction and communication skills than autistic males, which reflected the pattern found for nonautistic individuals. Both autistic females and

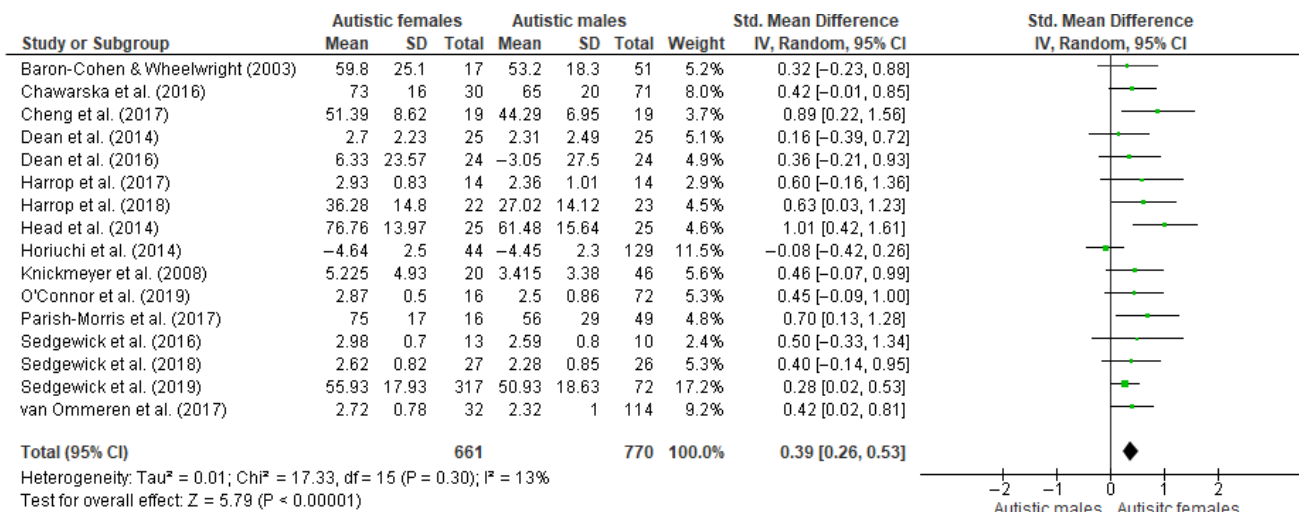


Figure 2 Forest plot for meta-analysis comparing autistic males and females on narrow construct measures of social interaction and communication

males had significantly lower social interaction and communication than their nonautistic female and male counterparts. The difference between nonautistic males with nonautistic females, and autistic females with nonautistic females became more evident with increased age. Finally, nonautistic males had better social interaction and communication than autistic females, though this difference was not statistically significant.

Three previous meta-analyses found no significant social interaction and communication differences between autistic males and females (Hull et al., 2017; Mahendiran et al., 2019; van Wijngaarden-Cremers et al., 2014), based upon data predominantly derived from diagnostic instruments (e.g. ADOS-2). Researchers have argued that a focus on diagnostic instruments may be biased towards a male-specific manifestation of ASD (Lai et al., 2015;

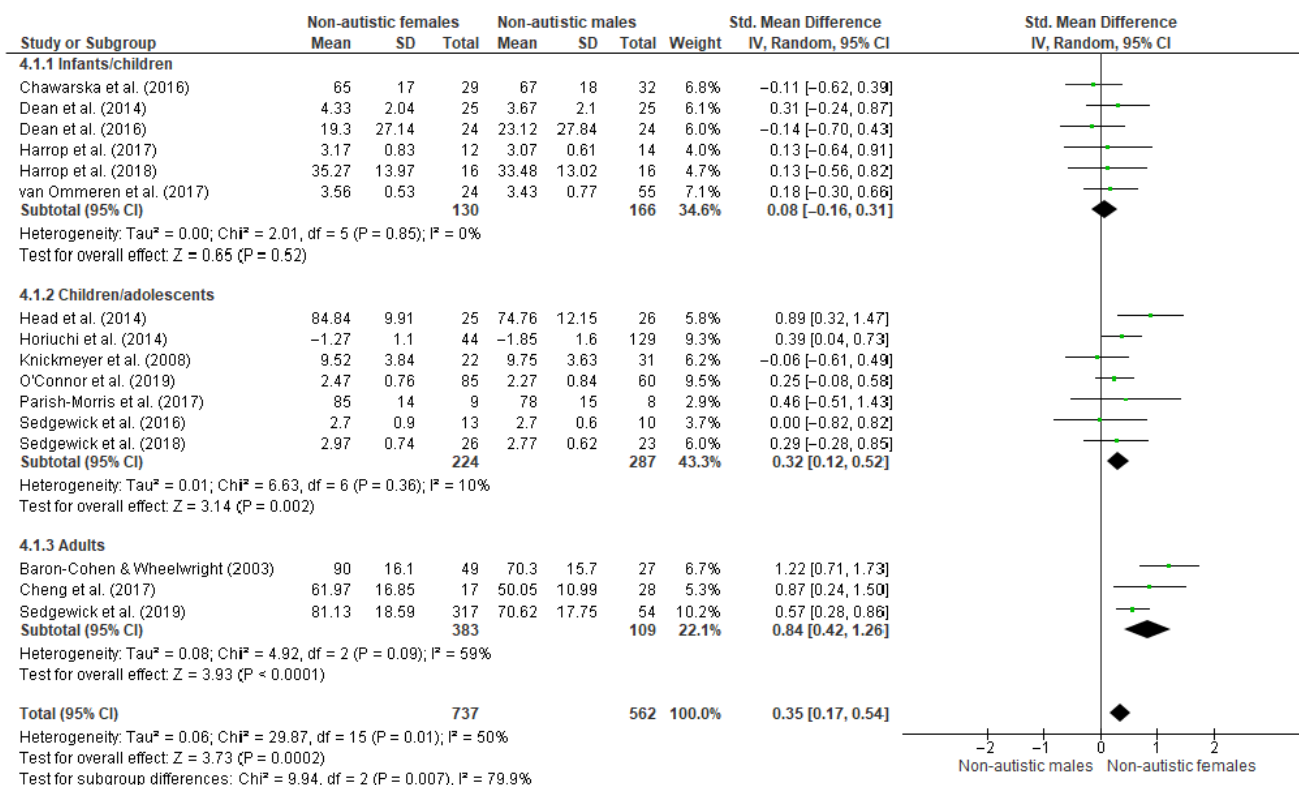


Figure 3 Forest plot and moderator analysis for meta-analysis comparing nonautistic males and females on narrow construct measures of social interaction and communication

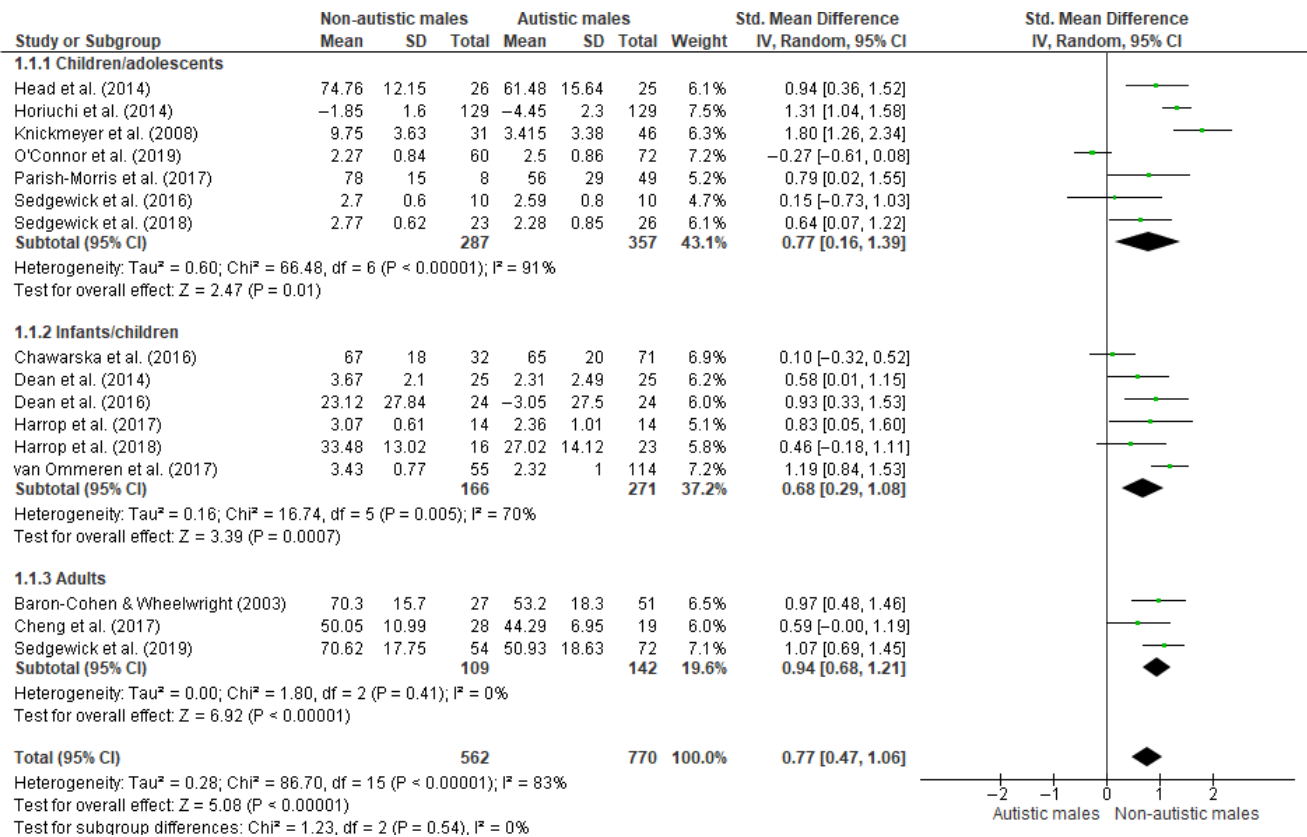


Figure 4 Forest plot and moderator analysis for meta-analysis comparing autistic and nonautistic males on narrow construct measures of social interaction and communication

Lai & Szatmari, 2020). Following Lai et al. (2015) and Lai and Szatmari (2020), our analysis of sex/gender differences only included narrow construct measures of social interaction and communication, and a significant difference between autistic males and females was found in these domains. Significantly, although the majority of females within our sample had met diagnostic criteria for ASD and therefore broadly shared a similar set of difficulties to autistic males, sex/gender differences were apparent when examined on narrow construct variables (Lai et al., 2015). This sex/gender difference suggests that, in certain social and communication domains, autism manifests differently in males and females. Moreover, the finding indicates that these differences may not be captured by pre-existing diagnostic instruments and potentially contribute to the under recognition of autism in females (Halladay et al., 2015; Lai & Szatmari, 2020).

The sex/gender difference supports the proposition raised by previous studies that autistic females are better able to camouflage social difficulties (e.g. Hull et al., 2019; Wood-Downie et al., 2020). Specifically, this interpretation is consistent with research that has found autistic females presenting as behaviourally more advanced than autistic males in certain contexts, despite having similar levels of underlying social-cognitive difficulties, and that this difference is likely to contribute to the under

recognition and later diagnosis of females (Hull et al., 2020 for a review; Lai et al., 2016). Another interpretation of these findings is that the more advanced social interaction/communication profile in autistic females reflects normative sex/gender differences. Consistently, the current findings indicated that nonautistic females also had more advanced social interaction and communication skills than nonautistic males, and the SMD within autistic and nonautistic groups was similar.

In the current findings, heterogeneity tests indicated that there was significant variation in all analyses, apart from the comparison between autistic males and females. In the context of heterogeneity, age was found to be a significant moderating variable in two comparisons: autistic and nonautistic females, and nonautistic males and females. In terms of autistic and nonautistic females, the difference between these groups increased in a stepwise manner, such that nonautistic females demonstrated better social interaction and communication than autistic females as they got older (which was not found when comparing autistic and nonautistic males). This finding is consistent with results from a recent longitudinal study which found that adolescence was associated with an increase in autistic traits for females without a clinical diagnosis (and not males) (Mandy, Pellicano, St Pourcain, Skuse, & Heron, 2018). The findings support the adolescent

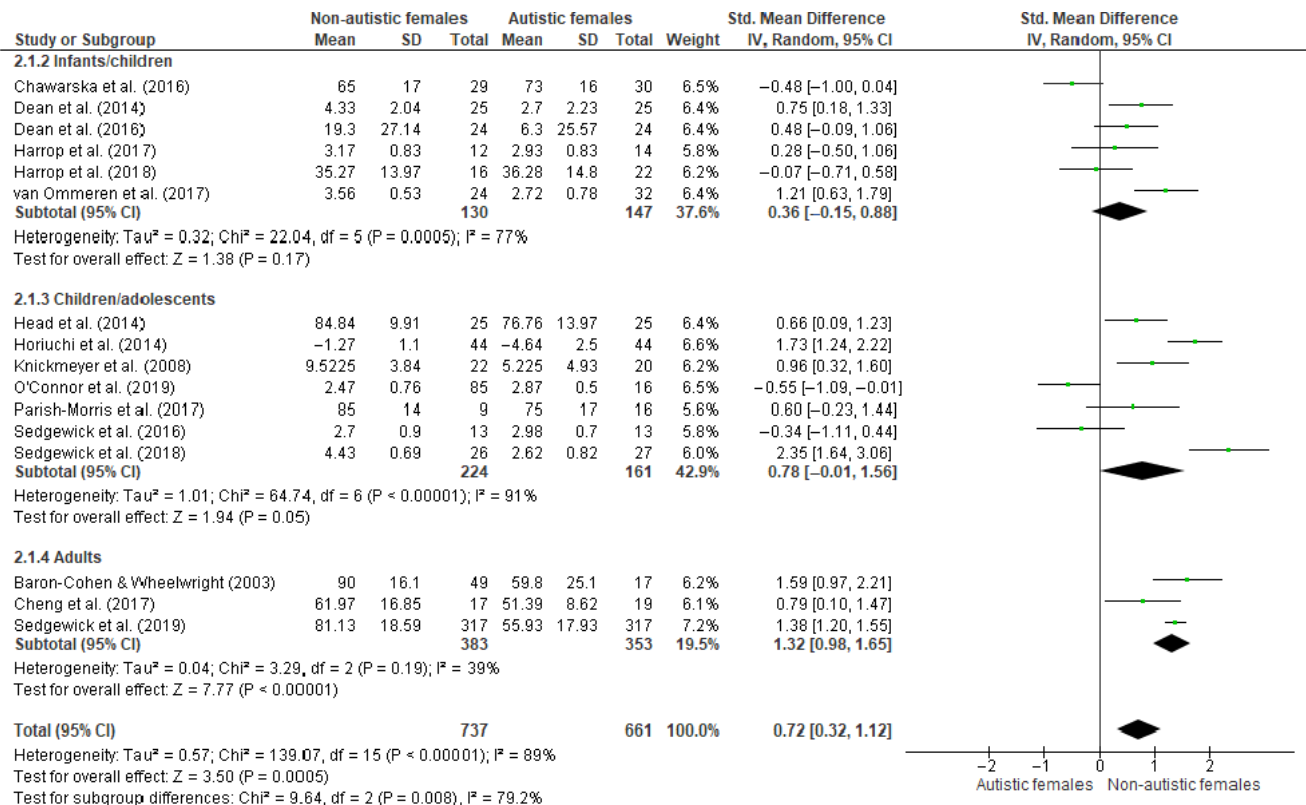


Figure 5 Forest plot and moderator analysis for meta-analysis comparing autistic and nonautistic females on narrow construct measures of social interaction and communication

emergence hypothesis, that autistic traits in females become most evident in adolescence. Collectively, these results suggest that autism associated developmental difficulties become more visible with age. One interpretation is that camouflaging strategies may no longer be sufficient to meet increased social demands in adolescence, and this difficulty may be particularly pronounced for female adolescents (e.g. Cridland, Jones, Caputi, & Magee, 2014). A similar stepwise pattern was found for the comparison between nonautistic males and females, suggesting that better social and communication skills become more pronounced through development.

Autistic females had significantly better social interaction and communication than autistic males, which mirrored sex/gender differences found for nonautistic individuals. In addition, although nonautistic males had more advanced social communication and interaction than autistic females, this difference was nonsignificant, suggesting that females with social communication difficulties may be overlooked when being compared to males (with and without autism). Therefore, practitioners may want to more carefully consider normative sex/gender differences when assessing social and communication difficulties by comparing to same-gender peers (Hull et al., 2017). For example, a female with underlying social difficulties may appear behaviourally similar to nonautistic males – and more advanced than autistic males – in the same setting

(e.g. class), perhaps making her less likely to be referred for assessment and given appropriate support.

The current findings indicate that reflection is needed in regard to potential implications for the diagnostic process. For example, increased social interaction and communication skills based on narrow construct measures evident for autistic females suggests that adjusting diagnostic criteria (e.g. having lower cut-off scores for females than males) may be important to account for these differences (Hull et al., 2017; Lai et al., 2015). The moderating impact of age for some analyses (e.g. highlighting that the difference between autistic and nonautistic females increased as individuals got older) further suggests that lowering cut-off scores in the diagnostic process may be more important for younger (vs. older) females.

The current findings have implications for understanding sex/gender in the ASD diagnostic process; however, our findings are limited to narrow construct measures, and not pre-existing diagnostic instruments. Indeed, a recent large-scale and multi-site analysis found no social interaction and communication differences between autistic males and females based upon the ADOS and ADI-R (Kaat et al., 2020), providing some evidence that sex/gender dependent cut-off scores are unnecessary. Kaat et al. (2020) acknowledged, however, that a major limitation of their analysis was the inclusion of

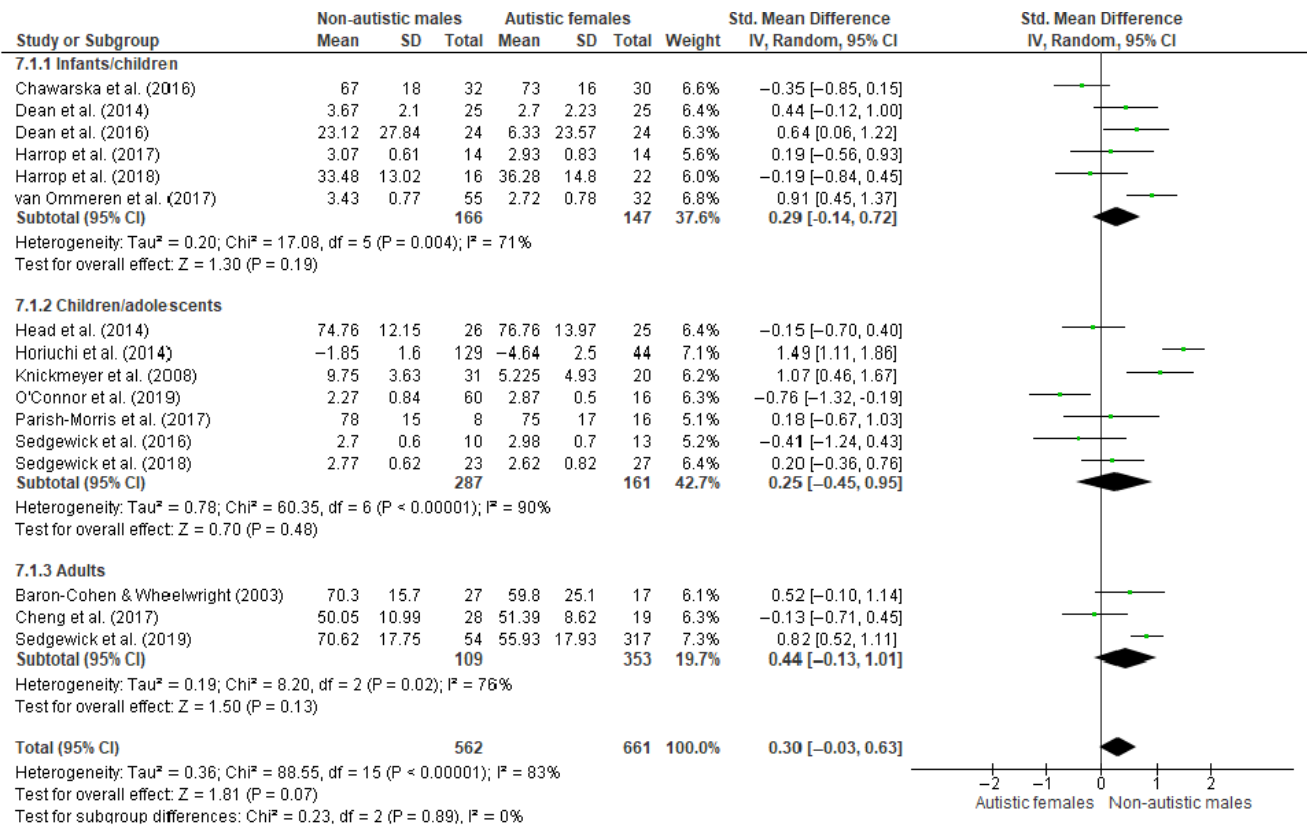


Figure 6 Forest plot and moderator analysis for meta-analysis comparing autistic females and nonautistic males on narrow construct measures of social interaction and communication

only individuals who already had clinical diagnoses of ASD. Specifically, the authors recognized that they were unable to evaluate sensitivity and specificity of these diagnostic instruments, particularly for those individuals who have milder ASD and/or differing behavioural presentations, which could include females. This illustrates the fundamental importance of future studies including participants who have not yet come to clinical attention, but who have high levels of autistic traits and who would meet ASD diagnostic threshold (i.e. using active case ascertainment methods), as well as including nonautistic male and female comparison groups, in order to make more substantive claims about diagnostic criteria and thresholds.

Strengths, limitations, and avenues for future research

This systematic review and meta-analysis represents a novel exploration of sex/gender differences in narrow construct measures of social interaction and communication between autistic and nonautistic male and female comparison groups. It addressed potential sex/gender diagnostic biases by extending existing reviews to exclude studies based only on pre-existing diagnostic instruments. The findings highlighting sex/gender differences in social

interaction and communication are significant in developing our understanding of autism in females, with the aim of providing tailored intervention and support. In addition, they may help inform the diagnostic process with respect to understanding the social and communication profile between sex/gender.

One limitation of the meta-analysis is the relatively small number of studies included. The number of studies meant that we were not able to quantitatively estimate publication bias for four analyses, and the moderation analyses were relatively underpowered. In addition, some heterogeneity tests remained significant after moderator analysis, suggesting that future research should aim to understand other factors that could influence the magnitude of sex/gender differences in autism. Factors may include the type of social and communication measure used (e.g. questionnaire vs. behavioural task), the specific narrow construct under investigation and the impact of any IQ differences (e.g. Loomes et al., 2017; Rutter, Caspi, & Moffitt, 2003). For example, previous studies have found that sex/gender differences are influenced by differences in IQ, where fewer females are diagnosed when considering individuals with higher IQ (Fombonne, 2009). Previous studies have also found that higher IQ is associated with greater levels of camouflaging (Livingston, Colvert,

Bolton, & Happé, 2018; Wood-Downie et al., 2020) and that camouflaging is more prevalent in females (e.g. Lai et al., 2016). Therefore, it is plausible that females with higher IQ are better able to camouflage underlying social-cognitive difficulties, as evidenced by more advanced social communication and interaction skills (as found in the current analysis), thereby making them less likely to receive a diagnosis. Future studies should attempt to systematically address the relationship between sex/gender, social and communicative behavioural presentation, underlying social-cognitive ability and/or neurobiology (Livingston & Happé, 2017), IQ and likelihood of receiving a diagnosis.

In the current analysis, there was insufficient variability in IQ scores to investigate it as a potential moderating variable. Eight studies reported IQ and only one (Sedgewick et al., 2016) included participants with an IQ < 80. In all of the remaining studies, IQ scores were within the average range (88–110). Future research should investigate IQ as a potential moderating variable of sex/gender differences in narrow construct social communication and interaction variables. Additionally, there is a possibility of bias resulting from gender stereotypes in the present results. For example, females with autism may be perceived as being ‘shy’ or ‘immature’, as opposed to experiencing social difficulties (Attwood, 2006; Kreiser & White, 2014). Some researchers have suggested that questionnaires may be particularly susceptible to these biases (Choi & Pak, 2004), reinforcing the need to employ more objective measurement tasks in the future for understanding sex/gender differences in autism (Lai et al., 2015).

Due to the limited number of studies, we were also unable to analyse separate subgroups for infants, toddlers, children and adolescents, and instead, we combined these into infant/children and children/adolescent groups, respectively. A lack of studies to enable a comparison of specific developmental stages may partly account for some of the residual heterogeneity and illustrates the need for more research to be conducted across the life span. Finally, four authors did not respond to requests for data.

Conclusion

This systematic review and meta-analysis investigated sex/gender differences in narrow construct measures of social interaction and communication based upon DSM-5 ASD diagnostic criteria. It provided evidence to support the proposition that females with ASD have more advanced social

interaction and communication than autistic males, which mirrored sex/gender differences found in nonautistic individuals. In addition, nonautistic males and females had better social interaction and communication than autistic males and females. Finally, nonautistic males had better social interaction and communication than autistic females, though this finding was not significant. These results develop our understanding of autism in females and go some way to explaining why girls with ASD are typically diagnosed at a later age than boys. We argue that the findings have potential implications for ASD diagnostic criteria. More research is needed to compare males and females with and without ASD on a broader range of narrow constructs, using active case ascertainment, and to investigate other potential moderating variables.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article:

Appendix S1. Further details of eligibility criteria.

Appendix S2. Further information about search results.

Appendix S3. Table 2 note.

Appendix S4. Further details of study quality.

Table S1. Search terms used.

Table S2. References and reasons for full-text article exclusion.

Figure S1. Funnel plot for analysis comparing autistic males and females.

Figure S2. Funnel plot for analysis comparing autistic and neurotypical males.

Figure S3. Funnel plot for analysis comparing and autistic and neurotypical females.

Figure S4. Funnel plot for analysis comparing neurotypical males and females.

Figure S5. Funnel plot for analysis comparing autistic females and nonautistic males

Acknowledgments

The author has declared that they have no competing or potential conflicts of interest.

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Key points

- Research suggests that autism manifests differently in males and females.
- Previous meta-analyses in social interaction and communication have focused on the level of the broad construct, and have tended to report minimal differences between sex/gender.
- To overcome diagnostic bias and capture more subtle sex/gender differences, we conducted the first systematic review and meta-analysis that has focused exclusively on narrow constructs, not measured using pre-existing diagnostic instruments.
- Female (versus male) children and adolescents with ASD had significantly better social interaction and communication.
- The findings develop our understanding of autism in females, provide some explanation for why females are often diagnosed at a later age, and have potential implications for sex/gender differences in the diagnostic processes.

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Accepted for publication: 16 September 2020